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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/512,568	02/24/00	HEIN M	TSRI-184.2Co

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EXAMINER	
BUI, P	
ART UNIT	**PAPER NUMBER**
1638	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Appl[illegible]
09/512,568	Hein et al.
Examiner	**Art Unit**
Phuong Bui	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 18, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-40 and 42-68* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *21-40 and 42-68* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Receipt is acknowledged of Applicant's Response, Amendment B, filed June 18, 2001. Claim 41 has been cancelled and new claims 65-68 have been entered. Accordingly, claims 21-40 and 42-68 are pending and are examined in the instant application. This action is made FINAL.

2. Sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3. Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the specification.

Double patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. The Office notes that Applicant indicates that appropriate Terminal Disclaimers will be filed to overcome the following obviousness-type double patenting rejections upon the indication of allowable subject matter.

6. The provisional rejection of claims 21-40 and 42-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-30 and 36-37 of copending Application No. 09/199534 is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

7. The provisional rejection of claims 21-40 and 42-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21 and 32-78 of copending Application No. 09/200657 is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

8. The rejection of claims 21-40 and 42-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-12 of U.S. Patent No. 5,959,177 is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

9. The rejection of claims 21-40 and 42-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,202,422 is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

10. The rejection of claims 21-40 and 42-64 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,639,947 is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

Claim Rejections - 35 USC § 112, second paragraph

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. The rejection of claims 30, 41, 52 and 61-63 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been obviated by Applicant's amendments and is hereby **withdrawn**.

Claim Rejections - 35 USC § 102

13. The rejection of claims 21, 22, 24-26, 29-39, 42-44, 46-48, 51-61 and 64 under 35 U.S.C. 102(b) as being anticipated by During (Dissertation, July 9, 1988, University of Koln, FRG, English translation), is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

During teaches a transgenic tobacco plant comprising cells which contain and express nucleotide sequences encoding an anti-NP-IgM antibody, which is a heteromultimeric protein. The antibody was glycosylated (p. 4 of English translation) and appears to be free of sialic acid residues. The antibody would inherently possess one or more disulfide bonds, hydrogen

bonding, Fab, Fab', F(ab')2, Fv, and J chain, and would contain a paratope. Accordingly, During anticipated the claimed invention.

Applicant's arguments have been fully considered, but were not found persuasive. Applicant asserts that During fails to anticipate the claimed invention as it fails to disclose transgenic plants including the claimed nucleotide sequences or the immunoglobulin products generated thereby. Applicants further assert that During fails to teach the requirement for cleavage of the leader sequence as is now claimed. Finally, Applicant asserts that During is non-enabling with regard to the production of an assembled, functional immunoglobulin in plant cells.

Regarding the assertion that During fails to teach the claimed nucleotide sequences or immunoglobulin products made therefrom, the Office notes that the claims do not recite specific nucleotide sequences. Thus, this argument is not germane to the claimed invention. Though the claims do recite a variety of immunoglobulin products, it is not clear which of these products set forth in one of the above included claims is not taught by During. During teaches the production of immunoglobulin molecules having both heavy and light chains.

Regarding Applicant's assertion of non-enablement of During, the Office notes that the burden of establishing non-enablement is Applicant's. In order to carry this burden, Applicant must produce evidence leading to the conclusion that one skilled in the art would have reasonably doubted that the the teaching of the reference would lead one skilled in the art to be able to make and use the disclosed subject matter in question. This standard does not require the

reference to "unquestionably" support the conclusions of the reference. Here, Applicant merely sets forth argument directing attention to portions of the During document. Applying this standard to these portions does not lead to the conclusion that the During document is non-enabling. The lack of corroboration that the Ac38 antibody is fully functional in itself does not lead to the conclusion that this antibody is in fact non-functional. Moreover, whether During required extremely sensitive assays for the presence of antibodies does not call the entire project into question. Again, to do so is to misapply the standard above. Finally, the fact that During suggests that additional experimentation is needed to confirm the results and/or to learn more about the nature of the expression and assembly of antibodies in plants also does not serve to establish non-enablement of this reference. It is common for researchers to raise questions and areas for further study when publishing their work. Such statements are not meant to show that the researchers conclusions are wrong and that ~~theri~~ their work cannot be duplicated with success. Thus, it is clear that Applicant has not carried the burden of establishing non-enablement of During.

14. The rejection of claims 21-27, 29-40, 42-49, 51-62 and 64 under 35 U.S.C. 102(e) as being anticipated by Goodman (US Pat. No. 4956282), is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

Goodman teaches transformation of monocots and dicots by introducing a vector containing nucleotide sequences encoding interferon (homomultimer), enzymes and immunoglobulin heavy and light chains for expressing immunoglobulins (heteromultimer) (col.

3, ln. 20-30). The antibody would inherently possess the Fab, Fab', F(ab)2, Fv and J chain regions, since these are all antibody components. The antibody would inherently bind a predetermined antigen and possess a paratope. The antibody of Goodman appears to be glycosylated (since Goodman desires retention of its biological activity) and free of sialic acid. Accordingly, absent of evidence to the contrary, Goodman anticipated the claimed invention.

Applicant's arguments have been fully considered, but were not found persuasive. Applicant asserts that Goodman also is non-enabled. Keeping in mind the standard set forth in the rejection above for an applicant to establish that a reference is non-enabled, the position of the Office is that Goodman may only be considered non-enabling for the production of fully assembled, complete antibodies when applied to claims of this scope. As none of the instant claims to which Goodman was applied recite the production of fully assembled, complete antibodies, Applicant's arguments must fail. In particular, Applicant notes that Goodman expresses single chain polypeptides in plant. Claims 44 and 66 specifically recite that the immunoglobulin molecule is only a single chain. Accordingly, Applicant's arguments regarding Goodman are not commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

15. The rejection of claims 21-40 and 42-64 under 35 U.S.C. 103(a) as being unpatentable over During (Dissertation, July 9, 1988, University of Koln, FRG, English translation), as applied to claims 21, 22, 24-26, 29-39, 42-44, 46-48, 51-61 and 64-68 above, and further in view of Applicant's admitted prior art.

The teachings of During have been discussed above. While During does not teach transformation of monocots or algae, transformation of these would have been well within the means of one of ordinary skill in the art without any surprising or unexpected results. It is noted that the examples are directed to transformation of a tobacco and the claims encompass monocots, algae and dicots. Also, while the antibody of During is a heteromultimeric protein (at least two different subunits), it would have been well within the means of one of ordinary skill in the art to make any known homomultimeric protein (at least two of the same subunits) based upon the teachings of During for making a heteromultimeric protein with a reasonable expectation of success, since the complexity and novelty of the invention lie with the multimeric protein property, rather than with the subunits per se. Again, it should be noted that the examples in Applicant's disclosure are directed to making an IgA antibody (heteromultimeric protein) and the claims encompass both heteromultimeric and homomultimeric proteins. The multimeric proteins which can expressed in plants based upon the teachings of During may or may not have enzymatic activity, since multimeric enzymes were notoriously well known in the prior art (p. 30). Further, while the antibody of During does not have catalytic activity (abzyme), it would have been obvious to transform plants using the method of During to express another desired antibody, such as abzymes of the prior art (specification, p. 30), without any surprising or unexpected results. Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to generate the claimed invention based upon the teachings of During with a reasonable expectation of success.

Applicant's arguments have been fully considered, but were not found persuasive. Applicant asserts that cell secretion in During is not observed as no association of antibody with the cell wall is observed. However, During teaches a leader sequence allowing for secretion of the expressed immunoglobulin molecule. Moreover, though Applicant argues that the During strategy is not commercially applicable, no such requirement is made either by the patent laws or by the instant claims. The only claim requiring a particular level of expression, claim 79, itself does not require that the expressed molecule be a fully assembled, complete antibody. Finally, since During teaches that fully assembled antibodies are produced, cleavage of the leader must have occurred. In addition, During discusses leader cleavage strategies thus suggesting to one of ordinary skill in the art other approaches to ensuring that the secretion signal would and should be cleaved.

16. The rejection of claims 21-40 and 42-64 under 35 U.S.C. 103(a) as being unpatentable over Goodman (US Pat. No. 4956282), as applied to claims 21-27, 29-40, 42-49, 51-62 and 64-68 above, and further in view of Applicant's admitted prior art, is hereby **maintained** and is further applied to new claims 65-68, for reasons of record.

The teachings of Goodman have been discussed above. While Goodman does not teach transformation of algae, such transformation would have been well within the means of one of ordinary skill in the art without any surprising or unexpected results. It is noted that the examples are directed to transformation of a tobacco and the claims encompass monocots, algae and dicots. Also, while the antibody of Goodman generically does not have catalytic activity

(abzyme), it would have been obvious to transform plants using the method of Goodman to express another desired antibody, such as abzymes of the prior art (specification, p. 30), without any surprising or unexpected results. It should also be noted that the antibody exemplified in the instant specification does not have enzymatic activity (abzyme). Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to transform monocots, algae or dicots, as well as express another antibody including abzymes using the method of Goodman with a reasonable expectation of success.

Applicant's arguments have been fully considered, but were not found persuasive. The comments set forth above are reiterated here. The instant claims do not all require fully assembled, complete antibodies that have been produced from plant cells. Thus, significantly, though the invention disclosed may require correct post-expression processing of expressed heavy and light chains, the claims do not make this requirement.

Remarks

17. No claim is allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant's amendment necessitated the new grounds of rejection. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Papers relating to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Bui whose telephone number is (703) 305-1996. The Examiner can normally be reached Monday-Friday from 6:30 AM - 4:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Phuong Bui
Primary Examiner
Group Art Unit 1638
August 25, 2001

Phuong Bui

PHUONG T. BUI
PRIMARY EXAMINER